```
=> d his

     (FILE 'HOME' ENTERED AT 09:19:32 ON 01 FEB 2007)

     FILE 'REGISTRY' ENTERED AT 09:20:06 ON 01 FEB 2007
                ACT KIS374A/A
L1              STR
L2              SCR 1950 AND 1994
L3              SCR 1363 OR 1236
L4              SCR 1838
L5   (      3307)SEA FILE=REGISTRY SSS FUL L1 AND L2 AND L3 NOT L4
L6              STR
L7            9 SEA FILE=REGISTRY SUB=L5 SSS FUL L6
               ---------

     FILE 'HCAPLUS' ENTERED AT 09:20:32 ON 01 FEB 2007
                E US20050095280/PN
L8            1 S E3
                SEL RN

     FILE 'REGISTRY' ENTERED AT 09:21:20 ON 01 FEB 2007
L9           12 S E1-E12

     FILE 'HCAPLUS' ENTERED AT 09:21:29 ON 01 FEB 2007
L10           1 S L8 AND L9

     FILE 'REGISTRY' ENTERED AT 09:21:45 ON 01 FEB 2007
L11           4 S L9 AND L7

     FILE 'HCAPLUS' ENTERED AT 09:22:02 ON 01 FEB 2007
L12           7 S L7
L13          25 S SAVVA M?/AU
L14          10 S L13 AND LIPID?
L15           6 S L12 NOT L14

     FILE 'USPATFULL' ENTERED AT 09:26:53 ON 01 FEB 2007
L16           3 S L7
L17           2 S L14
L18           2 S L16 NOT L17

     FILE 'TOXCENTER' ENTERED AT 09:27:40 ON 01 FEB 2007
L19           4 S L7
L20           1 S L14
L21           4 S L19 NOT L20

     FILE 'HCAPLUS' ENTERED AT 09:32:00 ON 01 FEB 2007


=> d que nos l14
L13          25 SEA FILE=HCAPLUS ABB=ON  PLU=ON  SAVVA M?/AU
L14          10 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L13 AND LIPID?


=> file uspatfull
FILE 'USPATFULL' ENTERED AT 09:35:18 ON 01 FEB 2007
CA INDEXING COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)

FILE COVERS 1971 TO PATENT PUBLICATION DATE: 30 Jan 2007 (20070130/PD)
FILE LAST UPDATED: 30 Jan 2007 (20070130/ED)
HIGHEST GRANTED PATENT NUMBER: US7171694
HIGHEST APPLICATION PUBLICATION NUMBER: US2007022507
CA INDEXING IS CURRENT THROUGH 30 Jan 2007 (20070130/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 30 Jan 2007 (20070130/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Aug 2006
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Aug 2006
```

```
=> d que nos l17
L13          25 SEA FILE=HCAPLUS ABB=ON  PLU=ON  SAVVA M?/AU
L17           2 SEA FILE=USPATFULL ABB=ON  PLU=ON  L13 AND LIPID?


=> file toxcenter
FILE 'TOXCENTER' ENTERED AT 09:35:31 ON 01 FEB 2007
COPYRIGHT (C) 2007 ACS


FILE COVERS 1907 TO 30 Jan 2007 (20070130/ED)

This file contains CAS Registry Numbers for easy and accurate substance
identification.

The MEDLINE file segment has been updated with 2007 MeSH terms.and
See HELP RLOAD for details.

TOXCENTER thesauri in the /CN, /CT, and /MN fields incorporate the
MeSH 2007 vocabulary.

=> d que nos l20
L13          25 SEA FILE=HCAPLUS ABB=ON  PLU=ON  SAVVA M?/AU
L20           1 SEA FILE=TOXCENTER ABB=ON  PLU=ON  L13 AND LIPID?


=> file hcaplus uspatfull toxcenter
FILE 'HCAPLUS' ENTERED AT 09:35:54 ON 01 FEB 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'USPATFULL' ENTERED AT 09:35:54 ON 01 FEB 2007
CA INDEXING COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'TOXCENTER' ENTERED AT 09:35:54 ON 01 FEB 2007
COPYRIGHT (C) 2007 ACS

=> dup rem l14 l17 l20
PROCESSING COMPLETED FOR L14
PROCESSING COMPLETED FOR L17
PROCESSING COMPLETED FOR L20
L22          10 DUP REM L14 L17 L20 (3 DUPLICATES REMOVED)
                ANSWERS '1-10' FROM FILE HCAPLUS

=> d ibib ed ab 1-10

L22  ANSWER 1 OF 10  HCAPLUS  COPYRIGHT 2007 ACS on STN DUPLICATE 1
ACCESSION NUMBER:         2005:394541  HCAPLUS  Full-text
DOCUMENT NUMBER:          142:435781
TITLE:                    Single-component pH-sensitive liposomes of
                          reduced solid-to-liquid phase transition
                          temperatures for gene delivery
INVENTOR(S):              Savva, Michalakis
PATENT ASSIGNEE(S):       Michalakis Savva, USA
SOURCE:                   U.S. Pat. Appl. Publ., 15 pp.
                          CODEN: USXXCO
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.        DATE
     ---------------      ----   --------    --------------------
     --------
     US 2005095280         A1    20050505    US 2003-686374
```

200310
15

PRIORITY APPLN. INFO.: US 2003-686374

200310
15

OTHER SOURCE(S): MARPAT 142:435781
ED Entered STN: 09 May 2005
AB The current invention relates to the synthesis of novel cationic **lipids** and their use as delivery vectors for nucleic acids, peptides and other synthetic drugs, in vitro and in vivo. The cationic **lipids** described herein form stable lamellar structures (liposomes) at physiol. pH but destabilize to micelles at acidic and alkaline pH. These structures are characterized by high elasticity, increased fluidity and high transfection activity relative to the corresponding 1,2-dialkyl cationic derivs. and other phospholipids analogs.

L22 ANSWER 2 OF 10 HCAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 2
ACCESSION NUMBER: 2005:346678 HCAPLUS Full-text
DOCUMENT NUMBER: 142:417187
TITLE: Cationic **lipids** for nucleic acid delivery
INVENTOR(S): **Savva, Michalakis**
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 8 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005084522	A1	20050421	US 2003-686262	200310 15

PRIORITY APPLN. INFO.: US 2003-686262 200310 15

OTHER SOURCE(S): MARPAT 142:417187
ED Entered STN: 22 Apr 2005
AB The invention describes the synthetic methods for a series of pH-sensitive cationic **lipids** with diamido linkages between the 1,2-diamino-3-propanol backbone and the hydrocarbon chains. Their in vitro biol. activity of the resulting **lipid**-DNA complexes is also described.

L22 ANSWER 3 OF 10 HCAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 3
ACCESSION NUMBER: 2003:423359 HCAPLUS Full-text
DOCUMENT NUMBER: 140:88218
TITLE: In vitro lipofection with novel series of symmetric 1,3-dialkoylamidopropane-based cationic surfactants containing single primary and tertiary amine polar head groups
AUTHOR(S): Sheikh, Mohammad; Feig, Jennifer; Gee, Becky; Li, Song; **Savva, Michalakis**
CORPORATE SOURCE: Arnold & Marie Schwartz College of Pharmacy and Health Sciences, Division of Pharmaceutics, Long Island University, Brooklyn, NY, 11201, USA
SOURCE: Chemistry and Physics of Lipids (2003), 124(1), 49-61
CODEN: CPLIA4; ISSN: 0009-3084
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

ED Entered STN: 03 Jun 2003
AB A novel series of sym. double-chained primary and tertiary 1,3-dialkoylamido monovalent cationic **lipids** were synthesized and evaluated for their transfection activities. In the absence of the helper **lipid** DOPE (1,2-dioleoyl-sn-glycero- 3-phosphoethanolamine), only the primary and tertiary dioleoyl derivs. 1,3lmp5 and 1,3lmt5, resp. elicited transfection activity. This is a striking difference between sym. 1,2-diacyl glycerol-based monovalent cationic **lipids** that always found both dioleoyl and dimyristoyl analogs being efficient transfection reagents. In the presence of helper **lipid**, all cationic derivs. induced marker gene expression, except the dilauroyl analogs 1,3lmp1 and 1,3lmt1 that elicited no transfection activity. Combining electrophoretic mobility data of the lipoplexes at different charge ratios with transfection activity suggested two requirements for high transfection activity with monovalent double-chained cationic **lipids**, i.e., binding/association of the **lipid** to the plasmid DNA and membrane fusion properties of the **lipid** layers surrounding the DNA.
REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 4 OF 10 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1162755 HCAPLUS Full-text
DOCUMENT NUMBER: 144:74592
TITLE: In Vitro Lipofection with Novel Asymmetric Series of 1,2-Dialkoylamidopropane-Based Cytofectins Containing Single Symmetric Bis-(2-dimethylaminoethane) Polar Headgroups
AUTHOR(S): **Savva, Michalakis**; Chen, Pensung; Aljaberi, Ahmad; Selvi, Bilge; Spelios, Michael
CORPORATE SOURCE: Division of Pharmaceutical Sciences, Arnold Marie Schwartz College of Pharmacy and Health Sciences, Long Island University, Brooklyn, NY, 11201, USA
SOURCE: Bioconjugate Chemistry (2005), 16(6), 1411-1422 CODEN: BCCHES; ISSN: 1043-1802
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 01 Nov 2005
AB Novel N,N'-diacyl-1,2-diaminopropyl-3-carbamoyl[bis-(2- dimethylaminoethane)] bivalent cationic **lipids** were synthesized and evaluated for in vitro transfection activity against a murine melanoma cell line. In the absence of the helper **lipid** DOPE (1,2-dioleoyl-sn-glycero-3-phosphoethanolamine), only the dioleoyl derivative 22 (1,21b5) elicited transfection activity. The transfection activity of this **lipid** was reduced when formulated with DOPE. Contrary to that, the dimyristoyl derivative 19 (1,21b2) mediated no activity when used alone but induced the highest levels of marker gene expression in the presence of DOPE. In an effort to correlate the transfection activity with cationic **lipid** structures, the physicochem. properties of cationic **lipids** in isolation and of lipoplexes were studied with surface tensiometry, photon correlation spectroscopy, gel electrophoresis mobility shift assay, and fluorescence techniques. In regard to the lipoplex properties, gel electrophoresis mobility shift assay and EtBr exclusion fluorescence assay revealed that the 1,21b5 was the only **lipid** to associate and condense plasmid DNA, resp. Photon correlation spectroscopy anal. found that 1,21b5/DNA complexes were of relatively small size compared to all other lipoplexes. With respect to the properties of isolated **lipids**, Langmuir monolayer studies and fluorescence anisotropy on cationic **lipid** dispersions verified high two-plane elasticity and increased fluidity of the transfection competent dioleoyl derivative 1,21b5, resp. The results indicate that high transfection activity is mediated by cationic **lipids** characterized by an expanded mean mol. area, high mol. elasticity, and increased fluidity.
REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 5 OF 10 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:25928 HCAPLUS Full-text
DOCUMENT NUMBER: 143:272152
TITLE: Synthesis, in vitro transfection activity and physicochemical characterization of novel

N,N'-diacyl-1,2-diaminopropyl-3-carbamoyl-(dimethylaminoethane) amphiphilic derivatives

AUTHOR(S): Aljaberi, Ahmad; Chen, Pensung; **Savva, Michalakis**

CORPORATE SOURCE: Division of Pharmaceutical Sciences, Arnold and Marie Schwartz College of Pharmacy and Health Sciences, Long Island University, Brooklyn, NY, 11201, USA

SOURCE: Chemistry and Physics of Lipids (2005), 133(2), 135-149
CODEN: CPLIA4; ISSN: 0009-3084

PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 12 Jan 2005

AB A novel series of N,N'-diacyl-1,2-diaminopropyl-3-carbamoyl- (dimethylaminoethane) cationic derivs. was synthesized and screened for in vitro transfection activity at different charge ratios in the presence and absence of the helper **lipids** DOPE and cholesterol. Physicochem. properties of **lipid**-DNA complexes were studied by gel electrophoresis, fluorescence spectroscopy and dynamic light scattering. The interfacial properties of the **lipids** in isolation were studied using the Langmuir film balance technique at 23 °C. It was found that only lipoplexes formulated with the dioleoyl derivative, 1,2lmt[5], mediated significant in vitro transfection activity. Optimum activity was obtained with 1,2lmt[5]/DOPE mixture at a ±charge ratio of 2. In agreement with the transfection results, 1,2lmt[5] was the only **lipid** found to complex and retard DNA migration as verified by gel electrophoresis. Despite the efficient complexation, no significant condensation of plasmid DNA was observed as indicated by fluorescence spectroscopy measurements. Monolayer studies showed that the dioleoyl derivative 1,2lmt[5] was the only **lipid** that existed in an all liquid-expanded state with a collapse area and collapse pressure of 59.5 Å2 and 38.7 mN/m, resp. This **lipid** was also found to have the highest elasticity with a compressibility modulus at monolayer collapse of 80.4 mN/m. In conclusion, increased acyl chain fluidity and high mol. elasticity of cationic **lipids** were found to correlate with improved transfection activity.

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 6 OF 10 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:503242 HCAPLUS Full-text

DOCUMENT NUMBER: 144:198343

TITLE: Correlation of the physicochemical properties of symmetric 1,3-dialkoylamidopropane-based cationic **lipids** containing single primary and tertiary amine polar head groups with in vitro transfection activity

AUTHOR(S): **Savva, Michalakis**; Aljaberi, Ahmad; Feig, Jennifer; Stolz, Donna Beer

CORPORATE SOURCE: Division of Pharmaceutical Sciences, Arnold and Marie Schwartz College of Pharmacy and Health Sciences, Long Island University, Brooklyn, NY, 11201, USA

SOURCE: Colloids and Surfaces, B: Biointerfaces (2005), 43(1), 43-56
CODEN: CSBBEQ; ISSN: 0927-7765

PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 13 Jun 2005

AB The physicochem. properties of a novel series of sym. 1,3-dialkylamidopropane-based cationic amphiphiles [M. Sheikh, J. Feig, B. Gee, S. Li, M. Savva, In vitro lipofection with novel series of sym. 1,3-dialkoylamidopropane-based cationic surfactants containing single primary and tertiary amine polar head groups, Chemical Phys. **Lipids** 124 (2003) 49-61] were studied by several techniques, in an effort to correlate cationic **lipid** structure with transfection efficacy. It was found that only the unsubstituted amine and tertiary amine dioleoyl derivs. 1,3lmp5 and 1,3lmt5, resp., mediated in vitro transfection activity in the absence of helper **lipids**. This activity

pattern was consistent with ethidium bromide fluorescence quenching studies, which indicated that only these two derivs. bound to and efficiently condense plasmid DNA at physiol. pH. Dynamic light scattering indicated that lipoplexes made by these two cationic **lipids** were relatively small particles below 1 μm, in sharp contrast to lipoplexes bigger than 3 μm composed of saturated cationic derivs. Transmission electron microscopy studies clearly indicated that cationic **lipid** dispersions made by saturated derivs. form multilamellar tubules at physiol. pH. Calorimetric studies showed that cationic amphiphiles with saturated acyl chains longer than 12 carbons exhibit solid-to-liquid crystalline phase transitions above 37 °C. In agreement with the microscopy and calorimetry studies, Langmuir film balance expts. indicated that saturated derivs. with hydrophobic chains longer that 12 carbons are not well hydrated and exist at a chain-ordered state at ambient temperature Calcn. of compressibility moduli from monolayer compression isotherms at 23 °C suggested that monolayers made by cationic **lipids** bearing saturated acyl chains are less compressible relative to those of the dioleoyl derivs. 1,3lmp5 and 1,3lmt5. In conclusion, high hydration, increased fluidity and high elasticity of cationic **lipid** assemblies in isolation, all correlate with high in vitro transfection activity.

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 7 OF 10 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:647605 HCAPLUS Full-text
DOCUMENT NUMBER: 132:46579
TITLE: Effect of PEG homopolymer and grafted amphiphilic PEG-palmityl on the thermotropic phase behavior of 1,2-dipalmitoyl-sn-glycero-3-phosphocholine bilayer
AUTHOR(S): **Savva, Michalakis**; Huang, Leaf
CORPORATE SOURCE: Departments of Pharmaceutical Sciences and Pharmacology, University of Pittsburgh, Pittsburgh, PA, 15261, USA
SOURCE: Journal of Liposome Research (1999), 9(3), 357-365
CODEN: JLREE7; ISSN: 0898-2104
PUBLISHER: Marcel Dekker, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 12 Oct 1999
AB Phospholipids covalently attached to polyethylene glycol (PEG-PE) are routinely used for the preparation of long-circulating liposomes. The common preparation procedure for long-circulating liposomes involves use of organic solvent. Although there is a plethora of studies describing the interaction of PEG-PE with bilayers, little is known about the effects of PEG homopolymers and single chain amphiphilic PEG on liposome structure. In the present investigation the interaction of PEG homopolymer and amphiphilic PEG-palmityl conjugate with large multilamellar liposomes composed of 1,2-dipalmitoyl-sn-glycero-phosphocholine was investigated utilizing differential scanning calorimetry. Vesicle and aggregate sizes were determined by dynamic light scattering. DSC thermograms revealed interaction of PEG homopolymer with DPPC when the two are premixed in organic solvent. The data suggest that PEG interacts with the phospholipid acyl chains deep in the bilayer. Several questions are raised regarding the suitability of the current procedure for preparation of long-circulating liposomes which utilizes organic solvent. Incorporation of only 2 mol% 5 kDa PEG-palmityl conjugate completely solubilized DPPC liposomes. Packing geometry of the **lipid** anchor, irresp. of the polymer mol. weight, is suggested to be the primary factor for successful grafting of hydrophilic polymers on liposomes. Pure PEG-palmityl formed self-assembled organized structures of potential use in the delivery of poorly soluble drugs.

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 8 OF 10 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:502263 HCAPLUS Full-text
DOCUMENT NUMBER: 131:327399
TITLE: Effect of Grafted Amphiphilic PVP-Palmityl

Polymers on the Thermotropic Phase Behavior of 1,2 Dipalmitoyl-sn-glycero-3-phosphocholine Bilayer

AUTHOR(S): **Savva, Michalakis**; Torchilin, Vladimir P.; Huang, Leaf

CORPORATE SOURCE: Departments of Pharmaceutical Sciences and Pharmacology, University of Pittsburgh, Pittsburgh, PA, 15261, USA

SOURCE: Journal of Colloid and Interface Science (1999), 217(1), 166-171
CODEN: JCISA5; ISSN: 0021-9797

PUBLISHER: Academic Press

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 12 Aug 1999

AB To better understand how grafted polymers interact with liposome membrane, a comparative study was conducted to investigate the influence of different chain length polyvinyl pyrrolidone-palmityl (PVP-p) conjugates on the thermotropic phase behavior of 1,2 dipalmitoyl-sn-glycero-3-phosphatidylcholine (DPPC) bilayer. **Lipid**-polymer dispersions were prepared by mixing DPPC and variable concns. of PVP-p conjugates in chloroform. Hydration of **lipids** was performed at 50-55°C after complete elimination of the organic solvent. DSC was used to determine **lipid** miscibility and bilayer-polymer interactions. Particle size was determined by photon correlation spectroscopy. Increasing concns. of 6 kDa PVP-p caused a shift of the main phase transition of DPPC at lower temps. At 9.1 mol% the DPPC phase pretransition (Tp) is abolished. At 16.7 mol%, differential scanning calorimetry showed an endothermic phase transition at 24.9°C. The enthalpy of this transition was twice as high compared to the main phase transition enthalpy of pure DPPC. Inclusion of more than 20 mol% of 6 kDa PVP-p resulted in a complete bilayer micellization. Qual. similar to the 6 kDa were the results obtained with the 12 kDa PVP-p conjugate. Increasing concns. of 25 kDa PVP-p from 1 to 13 mol% resulted in a decrease of the main DPPC phase transition temperature At 13 mol% the new mol. self-assembled structure as previously identified with the lower MW PVP-p conjugates also showed up at the DSC thermogram. However, in sharp contrast to the lower MW PVP-p conjugates, increasing the 25 kDa PVP-p content did not result in bilayer disruption; rather, it resulted in a bilayer stabilization. The consequences of the hydrophobically modified PVP interaction with the bilayer are considered neg. with respect to the long-circulating properties of liposomes in the blood. (c) 1999 Academic Press.

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 9 OF 10 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:502262 HCAPLUS Full-text

DOCUMENT NUMBER: 131:327398

TITLE: Effect of Polyvinylpyrrolidone on the Thermal Phase Transition of 1,2-Dipalmitoyl-sn-glycero-3-phosphocholine Bilayer

AUTHOR(S): **Savva, Michalakis**; Torchilin, Vladimir P.; Huang, Leaf

CORPORATE SOURCE: Departments of Pharmaceutical Sciences and Pharmacology, University of Pittsburgh, Pittsburgh, PA, 15261, USA

SOURCE: Journal of Colloid and Interface Science (1999), 217(1), 160-165
CODEN: JCISA5; ISSN: 0021-9797

PUBLISHER: Academic Press

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 12 Aug 1999

AB The purpose of this study was to investigate the interaction of polyvinyl pyrrolidone (PVP) with phospholipid bilayers in an effort to add a new dimension to our understanding of polymer interaction with **lipids**. For the preparation of **lipid**-polymer dispersions, measured amts. of DPPC (1,2 dipalmitoyl-sn-glycero-3- phosphocholine) and PVP were mixed in chloroform. After complete elimination of organic solvent, the dry mixts. were hydrated at 50-55°C. Interactions between DPPC and PVP were assessed by DSC and photon correlation spectroscopy (PS). Separation of liposomes and micelles was

performed by centrifugation. Liquid scintillation counting and a UV spectrophotometer were used for their anal. PVP added as dry powder or added as aqueous solution to dry lipid or preformed liposomes failed to interact. Only PVP previously dissolved in chloroform interacted with DPPC. The DPPC main phase transition moved to lower temps. with increasing PVP concns. This reduction of the phase transition temperature was accompanied by an increase of the DPPC phase transition enthalpy. Anal. of solubilization indicated that the amount of PVP present in the bilayer is dependent on the PVP bulk concentration The data suggest interaction of PVP previously dissolved in chloroform with the acyl chains of the phospholipid deep into the bilayer. (c) 1999 Academic Press.

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 10 OF 10 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:481727 HCAPLUS Full-text
DOCUMENT NUMBER: 129:235495
TITLE: PVP: a "pretender" molecule
AUTHOR(S): Savva, M.; Torchilin, V. P.; Huang, L.
CORPORATE SOURCE: University of Pittsburgh, Pittsburgh, PA, 15261, USA
SOURCE: Proceedings of the International Symposium on Controlled Release of Bioactive Materials (1998), 25th, 134-135
CODEN: PCRMEY; ISSN: 1022-0178
PUBLISHER: Controlled Release Society, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 04 Aug 1998
AB It appears that dipalmitoylphosphatidylcholine-PVP prepns. are stabilized through an enthalpic contribution. The observed lipid-polymer interaction is attributed to a change in the conformation of PVP, taking place during its dissoln. in organic solvent. Thus, PVP is a pretender mol. being able to acquire an appropriate conformation in a given environment. This can be of significant importance in formulations in which apolar solvents are used, e.g., transdermal and other topical dosage forms. In these formulations, the polymer might be presented in a hydrophobic conformation, thereby promoting keratinocyte barrier fluidization or interaction with living cells and other tissue components.
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d his nofile

(FILE 'HOME' ENTERED AT 09:19:32 ON 01 FEB 2007)

FILE 'REGISTRY' ENTERED AT 09:20:06 ON 01 FEB 2007
ACT KIS374A/A

L1 STR
L2 SCR 1950 AND 1994
L3 SCR 1363 OR 1236
L4 SCR 1838
L5 (3307) SEA SSS FUL L1 AND L2 AND L3 NOT L4
L6 STR
L7 9 SEA SUB=L5 SSS FUL L6

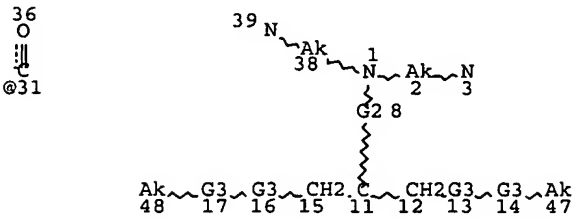
FILE 'HCAPLUS' ENTERED AT 09:20:32 ON 01 FEB 2007
E US20050095280/PN
L8 1 SEA ABB=ON PLU=ON US2005095280/PN
SEL RN

FILE 'REGISTRY' ENTERED AT 09:21:20 ON 01 FEB 2007
L9 12 SEA ABB=ON PLU=ON (112-64-1/BI OR 124-40-3/BI OR

```
                138404-83-8/BI OR 40538-81-6/BI OR 616-29-5/BI OR
                642475-14-7/BI OR 7693-46-1/BI OR 821-48-7/BI OR
                850785-34-1/BI OR 850785-35-2/BI OR 850785-36-3/BI OR
                850785-37-4/BI)

     FILE 'HCAPLUS' ENTERED AT 09:21:29 ON 01 FEB 2007
L10             1 SEA ABB=ON  PLU=ON  L8 AND L9

     FILE 'REGISTRY' ENTERED AT 09:21:45 ON 01 FEB 2007
L11             4 SEA ABB=ON  PLU=ON  L9 AND L7

     FILE 'HCAPLUS' ENTERED AT 09:22:02 ON 01 FEB 2007
L12             7 SEA ABB=ON  PLU=ON  L7
L13            25 SEA ABB=ON  PLU=ON  SAVVA M?/AU
L14            10 SEA ABB=ON  PLU=ON  L13 AND LIPID?
L15             6 SEA ABB=ON  PLU=ON  L12 NOT L14

     FILE 'USPATFULL' ENTERED AT 09:26:53 ON 01 FEB 2007
L16             3 SEA ABB=ON  PLU=ON  L7
L17             2 SEA ABB=ON  PLU=ON  L13 AND LIPID?
L18             2 SEA ABB=ON  PLU=ON  L16 NOT L17

     FILE 'TOXCENTER' ENTERED AT 09:27:40 ON 01 FEB 2007
L19             4 SEA ABB=ON  PLU=ON  L7
L20             1 SEA ABB=ON  PLU=ON  L13 AND LIPID?
L21             4 SEA ABB=ON  PLU=ON  L19 NOT L20

     FILE 'HCAPLUS' ENTERED AT 09:32:00 ON 01 FEB 2007
                D SCAN L10 TI
                D QUE NOS L14

     FILE 'USPATFULL' ENTERED AT 09:35:18 ON 01 FEB 2007
                D QUE NOS L17

     FILE 'TOXCENTER' ENTERED AT 09:35:31 ON 01 FEB 2007
                D QUE NOS L20

     FILE 'HCAPLUS, USPATFULL, TOXCENTER' ENTERED AT 09:35:54 ON 01 FEB
     2007
L22            10 DUP REM L14 L17 L20 (3 DUPLICATES REMOVED)
                     ANSWERS '1-10' FROM FILE HCAPLUS
                D IBIB ED AB 1-10

     FILE 'REGISTRY' ENTERED AT 09:36:38 ON 01 FEB 2007
                D QUE STAT L7

     FILE 'HCAPLUS' ENTERED AT 09:36:53 ON 01 FEB 2007
                D QUE NOS L15

     FILE 'USPATFULL' ENTERED AT 09:37:31 ON 01 FEB 2007
                D QUE NOS L18

     FILE 'TOXCENTER' ENTERED AT 09:37:44 ON 01 FEB 2007
                D QUE NOS L21

     FILE 'HCAPLUS, USPATFULL, TOXCENTER' ENTERED AT 09:38:20 ON 01 FEB
     2007
L23             8 DUP REM L15 L18 L21 (4 DUPLICATES REMOVED)
                     ANSWERS '1-6' FROM FILE HCAPLUS
                     ANSWERS '7-8' FROM FILE USPATFULL
                D IBIB ED ABS HITSTR 1-8

     FILE 'HCAPLUS' ENTERED AT 09:39:52 ON 01 FEB 2007
                D QUE NOS L14

     FILE 'USPATFULL' ENTERED AT 09:40:37 ON 01 FEB 2007
                D QUE NOS L17
```

```
FILE 'TOXCENTER' ENTERED AT 09:40:56 ON 01 FEB 2007
          D QUE NOS L20

FILE 'REGISTRY' ENTERED AT 09:41:10 ON 01 FEB 2007
          D QUE STAT L7

FILE 'HCAPLUS' ENTERED AT 09:41:23 ON 01 FEB 2007
          D QUE NOS L15

FILE 'USPATFULL' ENTERED AT 09:41:52 ON 01 FEB 2007
          D QUE NOS L18

FILE 'TOXCENTER' ENTERED AT 09:42:24 ON 01 FEB 2007
          D QUE NOS L21


=> file reg
FILE 'REGISTRY' ENTERED AT 09:36:38 ON 01 FEB 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2007 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   31 JAN 2007  HIGHEST RN 918932-71-5
DICTIONARY FILE UPDATES:  31 JAN 2007  HIGHEST RN 918932-71-5

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH June 30, 2006

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

=> d que stat l7
L1              STR

  N~Ak~N          Ak 4      Ak 5
  1  2  3


NODE ATTRIBUTES:
CONNECT IS E2  RC AT   2
DEFAULT MLEVEL IS ATOM
MLEVEL  IS CLASS  AT   2  4  5
GGCAT   IS SAT  AT   2
DEFAULT ECLEVEL IS LIMITED
ECOUNT  IS M11 C  AT   4
ECOUNT  IS M11 C  AT   5

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS   5

STEREO ATTRIBUTES: NONE
L2              SCR 1950 AND 1994
```

```
L3              SCR 1363 OR 1236
L4              SCR 1838
L5   (      3307)SEA FILE=REGISTRY SSS FUL L1 AND L2 AND L3 NOT L4
L6              STR
```




```
REP G2=(1-4) A
VAR G3=CH2/31/NH/S/O
NODE ATTRIBUTES:
CONNECT IS E2  RC AT   2
CONNECT IS E2  RC AT  38
DEFAULT MLEVEL IS ATOM
MLEVEL  IS CLASS  AT   2 38 47 48
DEFAULT ECLEVEL IS LIMITED
ECOUNT  IS M11 C  AT  47
ECOUNT  IS M11 C  AT  48

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  17

STEREO ATTRIBUTES: NONE
L7            9 SEA FILE=REGISTRY SUB=L5 SSS FUL L6

100.0% PROCESSED    3288 ITERATIONS                          9 ANSWERS
SEARCH TIME: 00.00.01


=> file hcaplus
FILE 'HCAPLUS' ENTERED AT 09:36:53 ON 01 FEB 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)

Copyright of the articles to which records in this database refer is
held by the publishers listed in the PUBLISHER (PB) field (available
for records published or updated in Chemical Abstracts after December
26, 1996), unless otherwise indicated in the original publications.
The CA Lexicon is the copyrighted intellectual property of the
the American Chemical Society and is provided to assist you in searching
databases on STN.  Any dissemination, distribution, copying, or storing
of this information, without the prior written consent of CAS, is
strictly prohibited.

FILE COVERS 1907 - 1 Feb 2007  VOL 146 ISS 6
FILE LAST UPDATED: 31 Jan 2007  (20070131/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=> d que nos l15
L1              STR
L2              SCR 1950 AND 1994
```

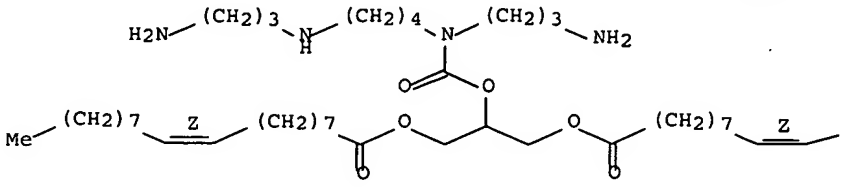
```
L3              SCR 1363 OR 1236
L4              SCR 1838
L5  (      3307)SEA FILE=REGISTRY SSS FUL L1 AND L2 AND L3 NOT L4
L6              STR
L7            9 SEA FILE=REGISTRY SUB=L5 SSS FUL L6
L12           7 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L7
L13          25 SEA FILE=HCAPLUS ABB=ON  PLU=ON  SAVVA M?/AU
L14          10 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L13 AND LIPID?
L15           6 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L12 NOT L14


=> file uspatfull
FILE 'USPATFULL' ENTERED AT 09:37:31 ON 01 FEB 2007
CA INDEXING COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)

FILE COVERS 1971 TO PATENT PUBLICATION DATE: 30 Jan 2007 (20070130/PD)
FILE LAST UPDATED: 30 Jan 2007 (20070130/ED)
HIGHEST GRANTED PATENT NUMBER: US7171694
HIGHEST APPLICATION PUBLICATION NUMBER: US2007022507
CA INDEXING IS CURRENT THROUGH 30 Jan 2007 (20070130/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 30 Jan 2007 (20070130/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Aug 2006
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Aug 2006


=> d que nos l18
L1              STR
L2              SCR 1950 AND 1994
L3              SCR 1363 OR 1236
L4              SCR 1838
L5  (      3307)SEA FILE=REGISTRY SSS FUL L1 AND L2 AND L3 NOT L4
L6              STR
L7            9 SEA FILE=REGISTRY SUB=L5 SSS FUL L6
L13          25 SEA FILE=HCAPLUS ABB=ON  PLU=ON  SAVVA M?/AU
L16           3 SEA FILE=USPATFULL ABB=ON  PLU=ON  L7
L17           2 SEA FILE=USPATFULL ABB=ON  PLU=ON  L13 AND LIPID?
L18           2 SEA FILE=USPATFULL ABB=ON  PLU=ON  L16 NOT L17


=> file toxcenter
FILE 'TOXCENTER' ENTERED AT 09:37:44 ON 01 FEB 2007
COPYRIGHT (C) 2007 ACS


FILE COVERS 1907 TO 30 Jan 2007 (20070130/ED)

This file contains CAS Registry Numbers for easy and accurate substance
identification.

The MEDLINE file segment has been updated with 2007 MeSH terms.and
See HELP RLOAD for details.

TOXCENTER thesauri in the /CN, /CT, and /MN fields incorporate the
MeSH 2007 vocabulary.

=> d que nos l21
L1              STR
L2              SCR 1950 AND 1994
L3              SCR 1363 OR 1236
L4              SCR 1838
L5  (      3307)SEA FILE=REGISTRY SSS FUL L1 AND L2 AND L3 NOT L4
L6              STR
L7            9 SEA FILE=REGISTRY SUB=L5 SSS FUL L6
L13          25 SEA FILE=HCAPLUS ABB=ON  PLU=ON  SAVVA M?/AU
L19           4 SEA FILE=TOXCENTER ABB=ON  PLU=ON  L7
L20           1 SEA FILE=TOXCENTER ABB=ON  PLU=ON  L13 AND LIPID?
L21           4 SEA FILE=TOXCENTER ABB=ON  PLU=ON  L19 NOT L20
```

```
=> file hcaplus uspatfull toxcenter
FILE 'HCAPLUS' ENTERED AT 09:38:20 ON 01 FEB 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'USPATFULL' ENTERED AT 09:38:20 ON 01 FEB 2007
CA INDEXING COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'TOXCENTER' ENTERED AT 09:38:20 ON 01 FEB 2007
COPYRIGHT (C) 2007 ACS

=> dup rem l15 l18 l21
PROCESSING COMPLETED FOR L15
PROCESSING COMPLETED FOR L18
PROCESSING COMPLETED FOR L21
L23             8 DUP REM L15 L18 L21 (4 DUPLICATES REMOVED)
                  ANSWERS '1-6' FROM FILE HCAPLUS
                  ANSWERS '7-8' FROM FILE USPATFULL

=> d ibib ed abs hitstr 1-8

L23  ANSWER 1 OF 8  HCAPLUS  COPYRIGHT 2007 ACS on STN DUPLICATE 1
ACCESSION NUMBER:         2006:259279  HCAPLUS  Full-text
DOCUMENT NUMBER:          145:152309
TITLE:                    Optimized lipopolyplex formulations for gene
                          transfer to human colon carcinoma cells under in
                          vitro conditions
AUTHOR(S):                Pelisek, Jaroslav; Gaedtke, Lars; DeRouchey,
                          Jason; Walker, Greg F.; Nikol, Sigrid; Wagner,
                          Ernst
CORPORATE SOURCE:         Department of Pharmacy, Center of Drug Research,
                          Pharmaceutical Biology-Biotechnology, Ludwig
                          Maximilian University, Munich, Germany
SOURCE:                   Journal of Gene Medicine (2006), 8(2), 186-197
                          CODEN: JGMEFG; ISSN: 1099-498X
PUBLISHER:                John Wiley & Sons Ltd.
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
ED   Entered STN:  21 Mar 2006
AB   Polycation (PC, polyplex), cationic lipid (CL, lipoplex), and a combination of PC/CL
     (lipopolyplex) formulations were investigated for gene transfer to slow-proliferating
     human colon carcinoma cell lines (COGA). The luciferase reporter gene was complexed
     with either PC, CL, or PC/CL. PCs included linear (PEI22lin, 22 kDa) and branched
     polyethylenimine (PEI2k, 2 kDa; PEI25br, 25 kDa) and poly-L-lysine (PLL18 with 18
     lysine monomers). CLs included DOCSPER, DOSPER and DOTAP. Lipopolyplexes were formed
     by either sequentially first mixing DNA with PC or CL, followed by addition of CL or
     PC, resp., or simultaneously with both PC and CL. Particle size and zeta-potential
     were determined and gene transfer and cytotoxicity were quantified on COGA-3. The
     highest gene transfer was achieved when DNA was first complexed with PC followed by CL.
     At low ionic strength, particles were small (50-130 nm) with a zeta-potential of +20-40
     mV. At physiol. ionic strength, only lipoplexes of DOCSPER or DOSPER and their resp.
     lipopolyplexes with PEI25br were stable to aggregation (140-220 nm). Lipopolyplexes of
     PEI25br were between 5- to 400-fold more efficient compared to the corresponding
     lipoplexes or polyplexes in all cases. Chloroquine did not significantly affect
     lipopolyplex-mediated gene transfer. Thus, lipopolyplex formulations of PEI25br in
     combination with multivalent CLs (DOCSPER, DOSPER) are promising tools for in vitro and
     potentially also in vivo gene transfer to colorectal cancer cells.
IT   203188-43-6
     RL: ADV (Adverse effect, including toxicity); PRP (Properties); THU
     (Therapeutic use); BIOL (Biological study); USES (Uses)
        (optimized lipopolyplex formulations for gene transfer to human
        colon carcinoma cells under in vitro conditions)
RN   203188-43-6  HCAPLUS
CN   9-Octadecenoic acid (9Z)-, 2-[[[(3-aminopropyl)[4-[(3-
```

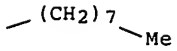
aminopropyl)amino]butyl]amino]carbonyl]oxy]-1,3-propanediyl ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 2 OF 8 HCAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 2
ACCESSION NUMBER: 2006:143562 HCAPLUS Full-text
DOCUMENT NUMBER: 144:445618
TITLE: Local gene transfer of C-type natriuretic peptide reduces restenosis and promotes proliferation of endothelial cells
AUTHOR(S): Kuehnl, A.; Pelisek, J.; Kopp, R.; Rolland, P.; Jauch, K.-W.; Nikol, S.
CORPORATE SOURCE: Chirurgische Klinik und Poliklinik Grosshadern, Ludwig-Maximilians-Universitaet, Munich, Germany
SOURCE: Chirurgisches Forum fuer Experimentelle und Klinische Forschung (2005) 1-2
CODEN: CFEKA7; ISSN: 0303-6227
PUBLISHER: Springer GmbH
DOCUMENT TYPE: Journal
LANGUAGE: German
ED Entered STN: 16 Feb 2006
AB C-type natriuretic peptide (CNP) reduces proliferation of smooth muscle cells (SMCs) and stimulates endothelial growth. The authors investigated the long-term therapeutic effects of adventitial liposome-mediated CNP gene or peptide application in a porcine restenosis model. For in vitro applications, primary cultures of porcine SMCs and endothelial cells (ECs) were used. Gene transfer was performed with cationic lipid DOCSPER. In vivo treatment of pig femoral arteries was adventitial using a needle injection catheter following balloon over-dilation in 11 pigs, 5 pigs served as controls. Arteries were then investigated using angiog., Evan's blue staining, histomorphometry, immunohistochem., PCR and RT-PCR at 3 wk or 3 mo. Using CNP gene transfer in vitro, 29 ± 7% reduction of cell proliferation in SMCs and 22 ± 6% enhancement of cellular growth in ECs was observed with minimal cytotoxicity of 5 ± 2%. CNP peptide demonstrated in SMC 50 ± 11 % reduction of cell proliferation with 30 ± 6% toxicity and 12 ± 5% enhancement of cellular growth of ECs without toxic effects. Three weeks following application in vivo Evan's blue staining demonstrated intactness of endothelium in controls and therapy groups. Minimal neointima formation was observed at 3 mo using CNP gene (CNP Plasmid 1,7 ± 0,4 % restenosis, CNP protein 5,6 ± 1,7% restenosis, control 15,6 ± 4,8% restenosis; $p < 0.05$). Periadventitial liposome-mediated CNP gene transfer in vivo resulted in rapid endothelial repair and significant long-term reduction of neointimal formation and was superior over single CNP peptide

administration. Advantages of CNP are its physiol. origin and simultaneous inhibition of SMC proliferation and promotion of EC growth.

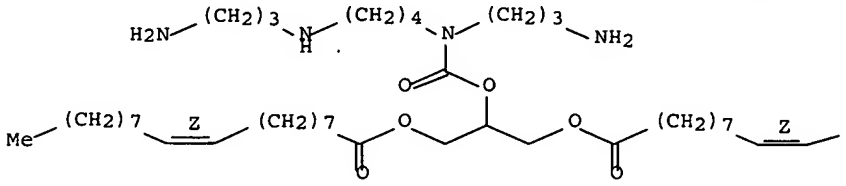
IT **203188-43-6**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(local gene transfer of C-type natriuretic peptide reduces restenosis and promotes proliferation of endothelial cells)

RN 203188-43-6 HCAPLUS

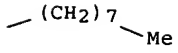
CN 9-Octadecenoic acid (9Z)-, 2-[[[(3-aminopropyl)[4-[(3-aminopropyl)amino]butyl]amino]carbonyl]oxy]-1,3-propanediyl ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 3 OF 8 HCAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 3

ACCESSION NUMBER: 2002:199221 HCAPLUS Full-text

DOCUMENT NUMBER: 137:57284

TITLE: Optimization of nonviral gene transfer of vascular smooth muscle cells in vitro and in vivo

AUTHOR(S): Armeanu, Sorin; Pelisek, Jaroslav; Krausz, Eberhard; Fuchs, Alexandra; Groth, Detlef; Curth, Rene; Keil, Oliver; Quilici, Jacques; Rolland, Pierre H.; Reszka, Regina; Nikol, Sigrid

CORPORATE SOURCE: Medical Clinic I, Klinikum Grosshadern, Ludwig Maximilian University, Munich, D-81377, Germany

SOURCE: Molecular Therapy (2000), 1(4), 366-375
CODEN: MTOHCK; ISSN: 1525-0016

PUBLISHER: Academic Press

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 19 Mar 2002

AB Gene therapy strategies for the prevention of restenosis postangioplasty are promising. Nonviral gene transfer to the arterial wall in vivo has so far been limited by poor efficiency. This study aimed to optimize transfection of primary vascular smooth muscle cells using cationic nonviral formulations based on cholesterol derivs. (DC-, DAC-, DCQ-, and Sp-Chol), double-chained amphiphiles (LipofectAMINE, DOTMA, DOSGA, DOSPER, and DOCSPER), or heterogeneous reagents (Superfect, Effectene, and Tfx-50). Estimation of transfection efficiencies was performed using galactosidase assays at different ratios of transfection reagent to plasmid DNA with reporter gene. Toxicity was monitored by analyzing cell metabolism Transfer efficiency and safety were determined

in a porcine restenosis model for local gene therapy using morphometry, histol., galactosidase assays, and reverse-transcriptase polymerase chain reaction. The highest in vitro transfection efficiency was achieved using the recently developed DOCSPER liposomes, with transfer rates of at least 20% in vascular smooth muscle cells. Transfer efficiency was further enhanced up to 20% by complexing with poly-L-lysine. Transfection efficiency in vivo in a porcine restenosis model was up to 15% of adventitial cells using DOCSPER vs. 0.1% using LipofectAMINE. Toxicity in vivo and in vitro was lowest using DOCSPER. Increased biol. effects were demonstrated following optimization of transfer conditions. (c) 2000 Academic Press.

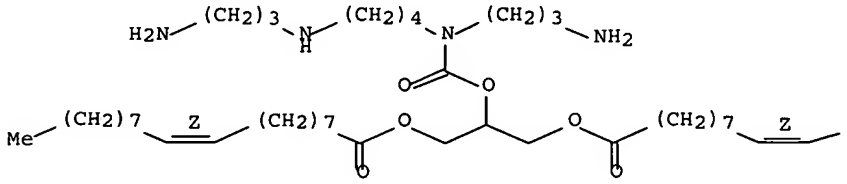
IT **203188-43-6**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(optimization of nonviral gene transfer of vascular smooth muscle cells in vitro and in vivo)

RN 203188-43-6 HCAPLUS

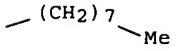
CN 9-Octadecenoic acid (9Z)-, 2-[[[(3-aminopropyl)[4-[(3-aminopropyl)amino]butyl]amino]carbonyl]oxy]-1,3-propanediyl ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 4 OF 8 HCAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 4

ACCESSION NUMBER: 1998:203964 HCAPLUS Full-text

DOCUMENT NUMBER: 128:326398

TITLE: Preparation and characterization of a new lipospermine for gene delivery into various cell-lines

AUTHOR(S): Groth, Detlef; Keil, Oliver; Lehmann, Cathleen; Schneider, Manfred; Rudolph, Michael; Reszka, Regina

CORPORATE SOURCE: Group Drug Targeting, Berlin-Buch, Max Delbruck Center for Molecular Medicine, Robert-Rossle-Strasse 10, Berlin, D-13125, Germany

SOURCE: International Journal of Pharmaceutics (1998), 162(1-2), 143-157
CODEN: IJPHDE; ISSN: 0378-5173

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 10 Apr 1998

AB A novel cationic amphiphile consisting of a hydrophobic 1,3-dioleoylglycerol moiety and a pos. charged spermine head group, 1,3-dioleoyloxy-2-(N5-carbamoylspermine)propane (DOCSPER), has been prepared Based on natural occurring materials, DOCSPER is susceptible to metabolic degradation and a promising agent for delivery of therapeutical genes in vivo. In aqueous solns. this lipospermine spontaneously forms liposomes with a size of about 20-100 nm. Liposomes composed of DOCSPER and the helper lipid dioleoylphosphatidylethanolamine (DOPE) were several hundred nm in size. DOCSPER liposomes were tested for their ability to transfect the rat glioblastoma cell-line F98, the rat colon carcinoma cell-line CC531, the T-cell line Jurkat and the human mamma tumor cell-lines MCF-7 and MaTu. Transfectability and toxicity of liposomes prepared with DOCSPER were compared with the Lipofectin reagent. Toxicity was significantly lower and transfection efficiencies were similar compared to Lipofectin. Lipid/DNA complex formation was controlled by turbidity measurements allowing easy determination of optimal lipid/DNA ratio for transfection.

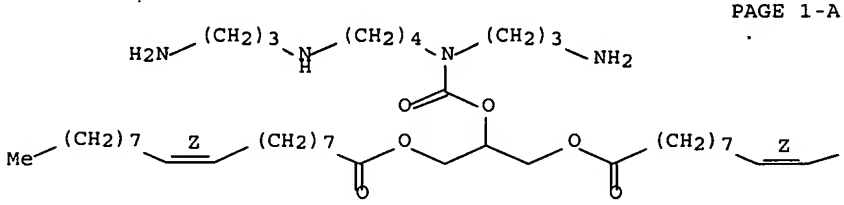
IT **203188-43-6P**
RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)
(preparation and characterization of a new lipospermine for gene delivery into various cell-lines)

RN 203188-43-6 HCAPLUS

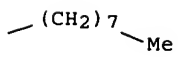
CN 9-Octadecenoic acid (9Z)-, 2-[[[(3-aminopropyl)[4-[(3-aminopropyl)amino]butyl]amino]carbonyl]oxy]-1,3-propanediyl ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



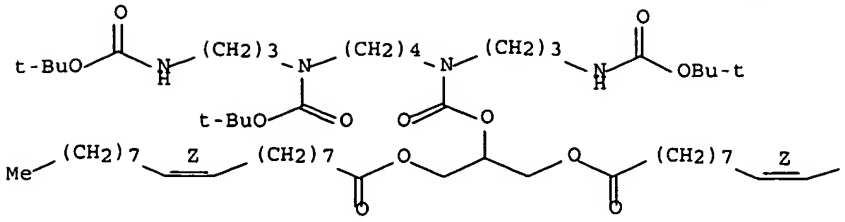
IT **203188-54-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and characterization of a new lipospermine for gene delivery into various cell-lines)

RN 203188-54-9 HCAPLUS

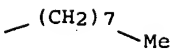
CN 2,6,11,15-Tetraazahexadecanedioic acid, 6-[(1,1-dimethylethoxy)carbonyl]-11-[[2-[[(9Z)-1-oxo-9-octadecenyl]oxy]-1-[[[(9Z)-1-oxo-9-octadecenyl]oxy]methyl]ethoxy]carbonyl]-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

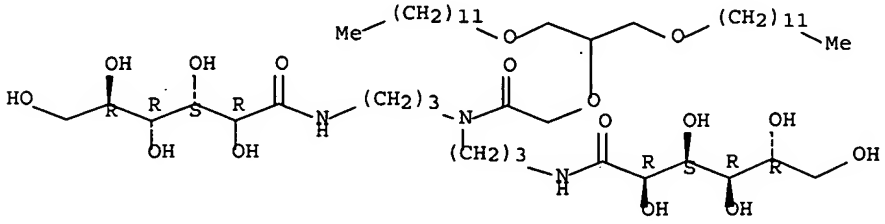
L23 ANSWER 5 OF 8 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:184738 HCAPLUS Full-text
DOCUMENT NUMBER: 141:309461
TITLE: Structural effects of amphiphiles on Candida rugosa lipase activation by freeze-drying of aqueous solution of enzyme and amphiphile
AUTHOR(S): Mine, Yurie; Fukunaga, Kimitoshi; Samejima, Ken-Ichi; Yoshimoto, Makoto; Nakao, Katsumi; Sugimura, Yoshiaki
CORPORATE SOURCE: Department of Applied Chemistry and Chemical Engineering, Faculty of Engineering, Yamaguchi University, Ube, 755-8611, Japan
SOURCE: Journal of Bioscience and Bioengineering (2003), 96(6), 525-528
CODEN: JBBIF6; ISSN: 1389-1723
PUBLISHER: Society for Biotechnology, Japan
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 08 Mar 2004
AB Lipases co-lyophilized with water-soluble gemini-type amphiphiles were found to have high enzyme activity in nonaq. media without washing out of the amphiphile with anhydrous organic solvent. In this study, we obtained freeze-dried complexes of Candida rugosa lipase (CRL) with six water-soluble twin glusitol-headed amphiphiles bearing different types of hydrophobic tails, including newly synthesized ones, and their transesterification activity in organic solvent was evaluated. The results indicate that the increased enzyme activity upon CRL modification at 200 molar ratio of amphiphile/CRL, which are restricted to the ester-containing amphiphiles, is probably due to the surface activation by the interaction between ester-carbonyl of the amphiphile and Ph group of the tyrosine residue situated on the surface of the lid in the CRL.
IT 766549-39-7, BIG 2C12OGly 766549-40-0, BIG 2C12OMeC
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(activation of Candida rugosa lipase using twin-headed

amphiphiles of nearly the same hydrophobicity with different alkyl chains)

RN 766549-39-7 HCAPLUS

CN D-Gluconamide, N,N'-[[[[2-(dodecyloxy)-1-[(dodecyloxy)methyl]ethoxy]acetyl]imino]di-3,1-propanediyl]bis-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

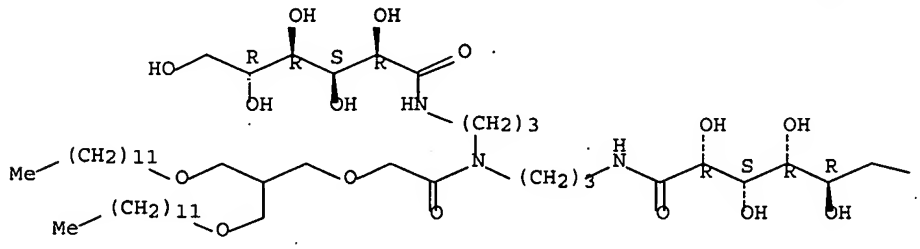


RN 766549-40-0 HCAPLUS

CN D-Gluconamide, N,N'-[[[[3-(dodecyloxy)-2-[(dodecyloxy)methyl]propoxy]acetyl]imino]di-3,1-propanediyl]bis-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

—OH

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 6 OF 8 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1998:102979 HCAPLUS Full-text

DOCUMENT NUMBER: 128:180582

TITLE: New cationic amphiphiles for liposomal gene transfer

INVENTOR(S): Schneider, Manfred; Keil, Oliver; Reszka, Regina; Groth, Detlef

PATENT ASSIGNEE(S): Max-Delbrueck-Centrum fuer Molekulare Medizin,

	Germany
SOURCE:	Ger. Offen., 26 pp.
	CODEN: GWXXBX
DOCUMENT TYPE:	Patent
LANGUAGE:	German
FAMILY ACC. NUM. COUNT:	1

PATENT INFORMATION:

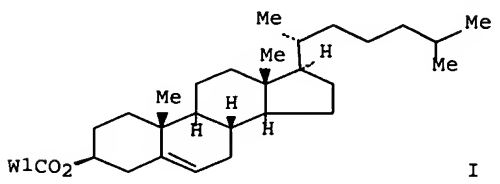
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19631189	A1	19980205	DE 1996-19631189	19960802
WO 9805678	A2	19980212	WO 1997-DE1669	19970801
WO 9805678	A3	19990225		
W: JP, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 923600	A2	19990623	EP 1997-936602	19970801
EP 923600	B1	20060621		
R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, NL, SE, FI				
JP 2000515861	T	20001128	JP 1998-507485	19970801
AT 330964	T	20060715	AT 1997-936602	19970801
US 6268516	B1	20010731	US 1999-230842	19990330
US 2002007073	A1	20020117	US 2001-898333	20010703
US 6489495	B2	20021203		

PRIORITY APPLN. INFO.:	DE 1996-19631189	A	19960802
	WO 1997-DE1669	W	19970801
	US 1999-230842	A3	19990330

OTHER SOURCE(S): MARPAT 128:180582

ED Entered STN: 20 Feb 1998

GI



I

AB Cationic amphiphiles, (R3COZCH2)CHYCOW [W = N{(CH2)nN+(R1)2R2}(CH2)mN+R1R2R3 2X-, CHR1NH2·HX, (CH2)nNHC(NH2):NH·HX; n = 2, 3, 4, 6, 8;m = 2, 3, 6, 8; R1 = H, Me, CH2CH2OH; R2 = H, Me, CH2CH2OH, (CH2)3N+(R1)3; R3 = linear, (un)saturated alkyl; Z = CH2, O, NH; Y = CH2, O, NH; X = Cl, Br, OAc, CF3CO2], and steroidal lipids I [W1 = N{(CH2)nN+(R1)2R2}(CH2)mN+(R1) 2R2 2X-, CHR1NHR2·HX, NH(CH2)mY] are described. Thus, cholesteryl lipid I·2HCl [W1 = CH(NH2)(CH2)3NH2] was prepared via reaction of Di-Boc-ornithine with cholesterol in CH2Cl2 containing DCC and DMAP followed by treatment with HCl in MeOH. These lipids are effective for liposomal gene transfer (data presented as graphs).

IT **203188-44-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of new cationic amphiphiles for liposomal gene transfer)

RN 203188-44-7 HCAPLUS

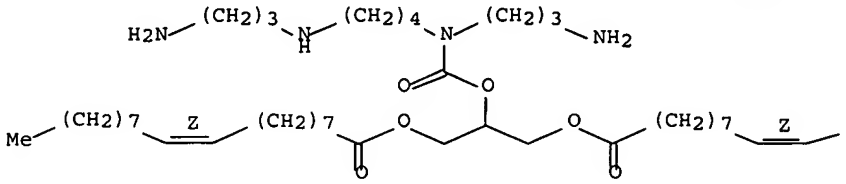
CN 9-Octadecenoic acid (9Z)-, 2-[[[(3-aminopropyl)[4-[(3-aminopropyl)amino]butyl]amino]carbonyl]oxy]-1,3-propanediyl ester, tris(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

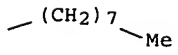
CRN 203188-43-6
CMF C50 H96 N4 O6

Double bond geometry as shown.

PAGE 1-A

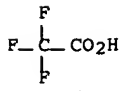


PAGE 1-B



CM 2

CRN 76-05-1
CMF C2 H F3 O2



IT **203188-54-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of new cationic amphiphiles for liposomal gene transfer)

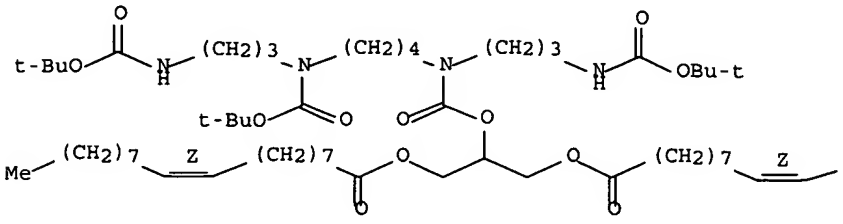
RN 203188-54-9 HCAPLUS

CN 2,6,11,15-Tetraazahexadecanedioic acid, 6-[(1,1-

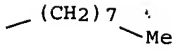
dimethylethoxy)carbonyl]-11-[[2-[[(9Z)-1-oxo-9-octadecenyl]oxy]-1-[[[(9Z)-1-oxo-9-octadecenyl]oxy]methyl]ethoxy]carbonyl]-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



L23 ANSWER 7 OF 8 USPATFULL on STN

ACCESSION NUMBER:	2002:12690 USPATFULL Full-text
TITLE:	Novel cationic amphiphiles for liposomal gene transfer
INVENTOR(S):	Schneider, Manfred, Wuppertal, GERMANY, FEDERAL REPUBLIC OF Keil, Oliver, Wuppertal, GERMANY, FEDERAL REPUBLIC OF Reszka, Regina, Schwanebeck, GERMANY, FEDERAL REPUBLIC OF Groth, Detlef, Ferch, GERMANY, FEDERAL REPUBLIC OF
PATENT ASSIGNEE(S):	Max-Delbruck-Centrum fur molekulare Medizin, Berlin, GERMANY, FEDERAL REPUBLIC OF (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002007073	A1	20020117
	US 6489495	B2	20021203
APPLICATION INFO.:	US 2001-898333	A1	20010703 (9)

RELATED APPLN. INFO.: Division of Ser. No. US 1999-230842, filed on 30 Mar 1999, GRANTED, Pat. No. US 6268516 A 371 of International Ser. No. WO 1997-DE1669, filed on 1 Aug 1997, UNKNOWN

	NUMBER	DATE
PRIORITY INFORMATION:	DE 1996-19631189	19960802

DOCUMENT TYPE:	Utility
FILE SEGMENT:	APPLICATION
LEGAL REPRESENTATIVE:	BRUCE LONDA, NORRIS, MCLAUGHLIN & MARCUS, P.A.,

220 EAST 42ND STREET, 30TH FLOOR, NEW YORK, NY, 10017
NUMBER OF CLAIMS: 9
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 6 Drawing Page(s)
LINE COUNT: 477
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention relates to the synthesis of novel cationic, amphiphilic lipids and their application as gene transfer vehicles in vitro and in vivo. For this a series of different lipids (diglycerides, steroids) were synthesized by modification with variable cationic molecules (amino acids, biogenic amines). Compounds of this kind are, due to their capability of producing complexes with polynucleotides (DNA, RNA, Antisense oligonucleotides, ribozymes etc) suitable as vectors for gene transfer (transfection).

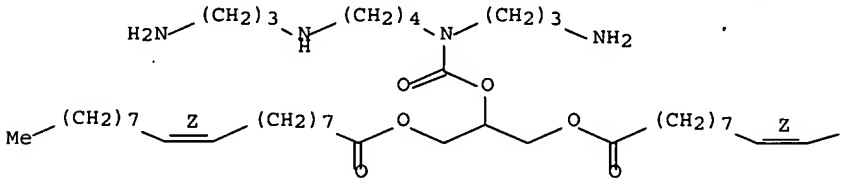
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **203188-44-7P**
(preparation of new cationic amphiphiles for liposomal gene transfer)
RN 203188-44-7 USPATFULL
CN 9-Octadecenoic acid (9Z)-, 2-[[[(3-aminopropyl)[4-[(3-aminopropyl)amino]butyl]amino]carbonyl]oxy]-1,3-propanediyl ester, tris(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

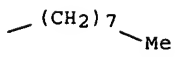
CRN 203188-43-6
CMF C50 H96 N4 O6

Double bond geometry as shown.

PAGE 1-A

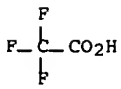


PAGE 1-B



CM 2

CRN 76-05-1
CMF C2 H F3 O2



IT **203188-54-9P**

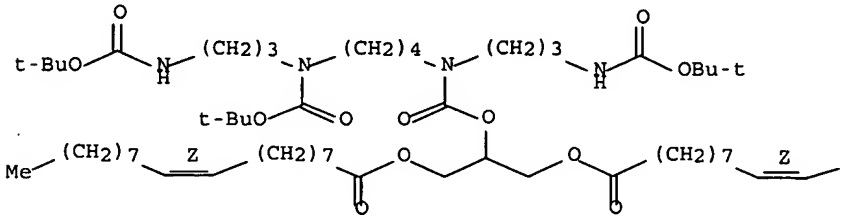
(preparation of new cationic amphiphiles for liposomal gene transfer)

RN 203188-54-9 USPATFULL

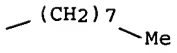
CN 2,6,11,15-Tetraazahexadecanedioic acid, 6-[(1,1-dimethylethoxy)carbonyl]-11-[[2-[[(9Z)-1-oxo-9-octadecenyl]oxy]-1-[[[(9Z)-1-oxo-9-octadecenyl]oxy]methyl]ethoxy]carbonyl]-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



L23 ANSWER 8 OF 8 USPATFULL on STN

ACCESSION NUMBER:	2001:121623 USPATFULL Full-text		
TITLE:	Cationic amphiphilic lipids for liposomal gene transfer		
INVENTOR(S):	Schneider, Manfred, Wuppertal, Germany, Federal Republic of Keil, Oliver, Wuppertal, Germany, Federal Republic of Reszka, Regina, Schwanebeck, Germany, Federal Republic of Groth, Detlef, Ferch, Germany, Federal Republic of		
PATENT ASSIGNEE(S):	Max-Delbruck-Centrum fur Molekulare Medizin, Germany, Federal Republic of (non-U.S. corporation)		
	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6268516	B1	20010731
	WO 9805678		19980212
APPLICATION INFO.:	US 1999-230842		19990330 (9)
	WO 1997-DE1669		19970801
			19990330 PCT 371 date
			19990330 PCT 102(e) date
	NUMBER	DATE	
PRIORITY INFORMATION:	DE 1996-19631189	19960802	
DOCUMENT TYPE:	Utility		

FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Badio, Barbara P.
LEGAL REPRESENTATIVE: Norris, McLaughlin & Marcus
NUMBER OF CLAIMS: 3
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 6 Drawing Figure(s); 6 Drawing Page(s)
LINE COUNT: 450
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention relates to the synthesis of novel cationic, amphiphilic lipids and their application as gene transfer vehicles in vitro and in vivo. For this a series of different lipids (diglycerides, steroids) were synthesized by modification with variable cationic molecules (amino acids, biogenic amines). Compounds of this kind are, due to their capability of producing complexes with polynucleotides (DNA, RNA, Antisense oligonucleotides, ribozymes etc) suitable as vectors for gene transfer (transfection).

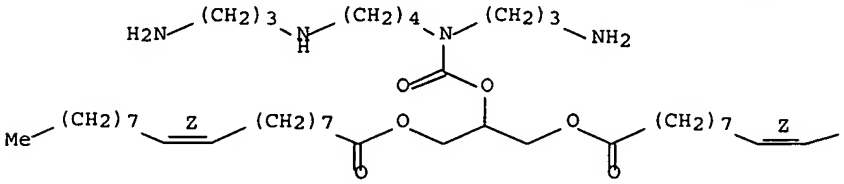
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **203188-44-7P**
(preparation of new cationic amphiphiles for liposomal gene transfer)
RN 203188-44-7 USPATFULL
CN 9-Octadecenoic acid (9Z)-, 2-[[[(3-aminopropyl)[4-[(3-aminopropyl)amino]butyl]amino]carbonyl]oxy]-1,3-propanediyl ester, tris(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

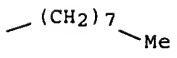
CRN 203188-43-6
CMF C50 H96 N4 O6

Double bond geometry as shown.

PAGE 1-A

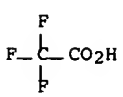


PAGE 1-B



CM 2

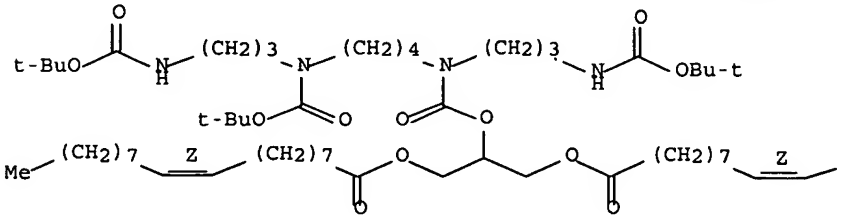
CRN 76-05-1
CMF C2 H F3 O2



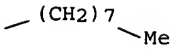
IT 203188-54-9P
(preparation of new cationic amphiphiles for liposomal gene transfer)
RN 203188-54-9 USPATFULL
CN 2,6,11,15-Tetraazahexadecanedioic acid, 6-[(1,1-dimethylethoxy)carbonyl]-11-[[2-[[(9Z)-1-oxo-9-octadecenyl]oxy]-1-[[[(9Z)-1-oxo-9-octadecenyl]oxy]methyl]ethoxy]carbonyl]-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



=>